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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/230,463	07/26/1999	DAVID WYNICK	23016.0002	4323

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EXAMINER	
GUCKER, STEPHEN	
ART UNIT	**PAPER NUMBER**
1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/230,463	Wysnick
Examiner	**Group Art Unit**
Stephen Gucker	1647

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☑ Responsive to communication(s) filed on 8/8/02.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

☑ Claim(s) 18-24 is/are pending in the application.

Of the above claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☑ Claim(s) 18-24 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

Attachment(s)

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☑ Notice of Reference(s) Cited, PTO-892

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Interview Summary, PTO-413

☐ Notice of Informal Patent Application, PTO-152

☐ Other _____

Office Action Summary

DETAILED ACTION

1. The request filed on 8/8/02 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/230,463 is acceptable and a CPA has been established. An action on the CPA follows.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Any objections or rejections made in a previous Office Action that are not herein reinstated have been withdrawn.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by

5. Claims 22-24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Concerning the breadth and limitations of the genus of galanin agonists used in the instant methods, the specification provides this definition:

> The term "galanin" embraces all known galanins including, for example, human, rat, murine and porcine galanin and also analogues of galanin having the biological activity of galanin (page 3).

As defined by Applicant, the term "galanin" encompasses all galanins found in different animal species as well as any analogues of such. Claims 22-24 claim the genus of processes or methods

of treatments wherein a galanin agonist is used but the agonist cannot be galanin itself. This is no literal support for this genus of processes in the disclosure as originally filed. Furthermore, the concept of methods of treatments using galanin agonists but excluding galanin itself as defined by the Applicant does not readily flow from any teachings set forth in the specification as originally filed. No galanin agonists other than galanin itself are taught *ipsis verbis* in the specification. This is a new matter rejection.

6. Claims 22-24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. No galanin agonists other than galanin itself as defined by the Applicant are described *ipsis verbis* in the specification. The Examiner has not found any art in the scientific or patent literature at the time of the foreign priority date afforded the instant Application (July 24, 1996) of galanin agonists that would not be encompassed by the term "galanin" as defined by the Applicant. This is a lack of an adequate written description rejection.

7. Claims 19-20 and 22-24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification teaches a mouse with targeted disruption of the galanin gene, experiments using the mouse, and the implication of the results of those experiments for the treatment of disease. In particular, the invention relates to the generation of a mutant mouse

carrying a loss-of-function germ-line mutation of the galanin locus. The mutation, when bred to homozygosity, affects feeding behaviour, lactation and pain sensitivity. The mutation *may* also affect memory and behaviour (page 2, italics added). Claims 19-20 and 23-24 are drawn to treatment of Alzheimer's disease (AD) or improving memory by administering galanin agonists (galanin itself is a galanin agonist). The specification does not provide adequate guidance or examples by which galanin agonists could be used to treat AD or improve memory because the art teaches that galanin agonists do not improve memory and are contraindicated for diseases such as AD (see the review article by Crawley, *Life Sci., Vol. 58*, May 10, 1996). The abstract for the review article by Crawley, which summarizes the work of many scientists in the field, clearly and unequivocally states that "centrally administered galanin inhibits acetylcholine release in rat ventral hippocampus, and produces deficits in learning and memory tasks." Also see pages 2192-2194 of Crawley where many experiments are described where galanin administration induces deficits on learning and memory tasks. Independently of Crawley, the Examiner also found an abstract by Liu et al. (*J. Neurotrauma, Vol. 11*, Feb. 1994) where the administration of galanin did not improve performance on a memory test, the Morris water maze, in rats with traumatic brain injury, but galanin did improve performance in sensory motor tests in brain damaged rats. The only scientific evidence that Applicants provide in support of enablement of methods of treating AD or improving memory by administering galanin to patients is by examining the long-term potentiation (LTP) of hippocampal brain slices taken from the galanin deficient mouse mutation that Applicants had invented. LTP is an electrophysiological measurement made from

brain slices of a sacrificed animal. The hippocampus is a brain region involved in memory function in both rodents and humans. Typically, increased LTP correlates with increased memory function in animal experiments. The instant disclosure teaches that hippocampal brain slices from the galanin deficient mutant mouse showed a 50% decrease in LTP as compared to non-galanin deficient normal control mice. The implication of this experiment, and the conclusion drawn by Applicants, is that by administering galanin, the deficit in LTP, and therefore impaired memory function, can be treated. However, the Examiner has discovered that this experimental conclusion has already been tested in the scientific literature and shown to be incorrect. Sakurai et al. (*Neurosci. Lett., Vol. 212*, July 5, 1996) administered galanin to guinea-pig hippocampal slices and discovered that galanin actually inhibits LTP. Because this direct experimental test of Sakurai et al. refutes the experimental prophetic prediction made by Applicants based on their mutant mouse model, and because the state of the art teaches that galanin agonists inhibit learning and memory, and because the state of the art teaches towards galanin antagonists and advises against galanin agonists for AD and other dementias, it is the Examiner's conclusion based on this evidence that claims 19-20 and 23-24 are not enabled by the instant disclosure because the invention claimed cannot be delivered into the hands of the artisan in a reasonably predictable manner given the lack of working examples disclosed and the existence of examples in the prior art that indicate that the instant invention as taught by the instant disclosure is in fact inoperative to the skilled artisan without unreasonable experimentation being required in order to render the invention as claimed as being enabled.

Claim 22 is not enabled because no galanin agonists other than galanin itself as defined by the Applicant are taught in the specification. The Examiner has not found any art in the scientific or patent literature at the time of the foreign priority date afforded the instant Application (July 24, 1996) of galanin agonists that would not be encompassed by the term "galanin" as defined by the Applicant. It would require unpredictable, undue experimentation to enable a method of using galanin agonists that are not galanin as defined by the Applicant because none were known to exist at the time of the invention.

8. Claims 18 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Luo et al. ("Luo"). Luo describes methods where galanin is administered to treat spinal cord hyperexcitability following sciatic nerve section which is peripheral nerve damage (abstract and pages 162-163).

9. Claim 18 is rejected under 35 U.S.C. 102(b) as being anticipated by Liu et al. ("Liu", abstract only). The abstract of Liu describes methods where galanin is administered to treat traumatic brain injury, and the administration of galanin lessens sensory motor deficits following brain injury, indicating its effectiveness.

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 18 and 21-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Luo in view of Kaplan (WO 92/12997). The teachings of Luo are set forth in **¶8** above. Luo does not teach methods using galanin agonists that are not galanin. Kaplan teaches the use of galanin agonists which are N-terminal fragments of galanin (page 5, lines 25-33). It would have been obvious to one of ordinary skill in the art at the time of the invention to use galanin fragments in lieu of galanin because galanin is a peptide. Peptides are bulky molecules made up of a chain comprising amino acids and possess epitopes that can cause immunological reactions when used pharmaceutically. The shorter the biologically active peptide chain (as in a fragment or partial chain), the easier and less expensive it is to manufacture by chemical peptide synthesis for a pharmaceutical composition and the fewer epitopes the shorter peptide chain has to react with the immune system and produce neutralizing antibodies. It would be *prima facie* obvious to utilize a method using a shorter peptide fragment as the biologically active ingredient because the method could be realized for less cost because a small fragment is easier and cheaper to manufacture than the complete peptide and would be less likely to produce an immunological reaction (neutralizing antibody production) in a subject than the larger peptide.

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Gucker whose telephone number is (703) 308-6571. The examiner can normally be reached on Monday to Friday from 0930 to 1800. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached

on (703) 308-4623. The fax phone number for this Group is currently (703) 308-4242, but Applicant should confirm this by phoning the Examiner before faxing.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

SG

Stephen Gucker

November 3, 2002

Gary L. Kunz

GARY KUNZ
SUPERVISORY PATENT EXAMINER
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